PERTUSSIS
(Whooping Cough)

✓DISEASE AND EPIDEMIOLOGY

Clinical description:

Pertussis is a highly contagious toxin-mediated bacterial disease that interferes with the body's ability to clear pulmonary secretions. Pertussis can be categorized into 3 stages.

- The first, the *catarrhal stage*, is characterized by non-specific respiratory symptoms with a worsening cough. It generally lasts 1-2 weeks.
- The *paroxysmal stage* is where most diagnosis occurs. Symptoms include sudden, severe coughing fits (paroxysms). These fits are often followed by a high-pitched whoop when the person breathes in. Persons may become cyanotic due to a lack of oxygen, and may vomit after a coughing fit. Infants and children generally have the most severe symptoms. In children under 6 months the most common symptom is apnea, and the whoop is often absent. Older children and adults may also lack the whoop, with a prolonged cough as the most common symptom. This paroxysmal stage can last for 1-6 weeks, sometimes lasting as long as 10 weeks.
- In the *convalescent stage*, the patient gradually recovers from the disease.

Subsequent respiratory infections may elicit paroxysms for months after the onset of pertussis. Milder disease is often seen in adolescents and adults and those who are partially protected because of vaccination.

Infants younger than 12 months are at the greatest risk of complications from pertussis infection. Bacterial pneumonia is the most common complication and cause of pertussis-associated deaths. The lack of oxygen caused by coughing can produce neurological disorders like seizures and encephalopathy (a dysfunction of the brain). Other complications include otitis media (ear infection), anorexia (loss of appetite), and dehydration. Complications resulting from pressure effects of severe paroxysms include pneumothorax (collection of gas or air in the chest cavity), epistaxis (nosebleed), subdural hematomas (swelling or mass of blood under the outer membrane covering the spinal cord), hernias (protrusion of organ through wall), and rectal prolapse (protrusion of rectal mucosa though the anus). Adolescents and adults may suffer from difficulty sleeping, urinary incontinence, pneumonia, and rib fracture.

Causative agent:

Pertussis is caused by *Bordetella pertussis*, a fastidious, gram-negative bacterium.

Differential diagnosis:

Typically, viruses cause upper respiratory infections/bronchitis. The frequency of pertussis as a cause of upper respiratory infection with prolonged cough varies, but can range from 5-20%. Other bacterial pathogens causing upper respiratory illnesses include *Bordetella parapertussis, Mycoplasma pneumoniae*, *Chlamydia trachomatis, Chlamydia pneumoniae, Bordetella bronchiseptica* and certain adenoviruses.

Laboratory identification:

Laboratory testing of pertussis can guide both clinical and public health responses. Pertussis can be easily missed and confused with other causes of chronic cough, so laboratory testing is useful in appropriate diagnosis. Additionally, laboratory data can significantly contribute to public health's ability to recognize an outbreak. However, laboratory testing can often be difficult, expensive, and may not be clinically useful. Laboratory testing may not be necessary in settings where the patient has clinically compatible symptoms and has exposure to a confirmed case, or where there is a documented outbreak in the community. Public health's recommendation for laboratory testing of individual cases should carefully consider the above circumstances, and should recognize that in certain situations, testing may not be necessary.

Serology:

Serologic diagnosis requires paired acute and convalescent sera and therefore it is not recommended for diagnosis due to the wait for convalescent sera. The use of a single serum specimen for diagnostic purposes is not well standardized outside of a research setting. Serology is best used to evaluate a person's immune response to vaccination. Serological tests should **never** be used as the sole laboratory method of pertussis diagnosis.

DFA:

While the speed of this test is appealing to determine antibiotic therapy, the sensitivity and specificity of this test are unacceptable. The majority of adults with pertussis will have negative DFA results.

PCR:

Currently, this test is the best option in most clinical circumstances. This test provides acceptable sensitivity in children and adults, has a relatively short turnaround time, and is available at most commercial reference laboratories. Nasopharyngeal swabs and aspirates are the preferred method for specimen collection. PCR results may not be reliable after 5 days of appropriate antibiotic treatment. Currently, no data are available as to how long patients with pertussis remain PCR positive. **NOTE:** NP swabs have thin wire shafts and are flexible. You cannot collect an NP specimen with a throat swab. Throat swabs and cough plates are not acceptable specimens.

Culture:

Culture is the gold standard for pertussis diagnosis. However, it is highly specific only in the initial stages of disease, and the sensitivity varies widely. Additionally, the length of time to obtain results makes it unacceptable for determining patient therapy. Nasopharyngeal swabs and aspirates are the preferred method for specimen collection. Pertussis DFA or PCR testing is always recommended in addition to culture. **NOTE:** NP swabs have thin wire shafts and are flexible. You cannot collect an NP specimen with a throat swab. Throat swabs and cough plates are not acceptable specimens.Generally this test may be used when:

- Testing children (sensitivity in adult patients is unacceptable)
- Using an on-site laboratory (transport decreases yield)
- Patients have not started taking antibiotics
- Patients are within two weeks of symptom onset
- Determining possible antibiotic resistance.
  UPHL: The Utah Public Health Laboratory can perform PCR. All isolates must be submitted to UPHL.

Treatment:

While antibiotics will eradicate the carriage of *Bordetella pertussis,* thereby decreasing communicablility, the extent to which antibiotics reduce the duration and severity of illness is unknown. It is widely believed that antibiotics started early in the course of illness are more likely to reduce the illness duration and severity than antibiotics started late in the course of illness. Public health recommends limiting antibiotic treatment to those who are within three weeks of the onset of their illness unless they are:

- Infants under the age of 1
- Pregnant women
- Patients with ongoing, close contact with infants under the age of 1 or pregnant women (e.g., parents and caregivers of infants, daycare workers, pediatricians)

Therapy recommended by the CDC in the 2005 revision of Guidelines for Control of Pertussis Outbreaks:

Drug	Infants <1 month	Children 1-6 months	Children > 6 months	Adults	Duration
Azithromycin	10 mg/kg/day in a single daily dose[1,7]	Not licensed, but may be used. 10 mg/kg/day in a single daily dose[1]	10 mg/kg in a single dose (day one); then 5 mg/kg per day in a single dose, (days 2-5) (maximum 500 mg/day)	500 mg in a single dose, day one; then 250 mg in a single dose, days 2-5[3]	5 days
Erythromycin[8]	2nd line choice. See children > 6 months for dosing[1]	See children > 6 months for dosing[1]	40-50 mg/kg per day, in 4 divided doses (maximum 2 g/day)	250 - 500 mg, 4 times per day[2]	14 days
Clarithromycin	Not recommended.	Not licensed, but may be used. See children > 6 months for dosing. [1]	15 mg/kg per day, in 2 divided doses (maximum 500 mg/dose)	500 mg, twice daily[4]	7 days
TMP/SMZ			8 mg/kg per day (TMP) 40 mg/kg per day (SMZ), in 2 divided doses	1 DS tablet, twice daily[6]	14 days

[1]An association between orally administered erythromycin and infantile hypertrophic pyloric stenosis (IHPS) in neonates has been reported.
[2]Erythromycin is classified as an FDA Pregnancy Category B drug.
[3]Azithromycin is classified as an FDA Pregnancy Category B drug.
[4]Clarithromycin is classified as an FDA Pregnancy Category C drug.
[5]TMP/SMZ may be used as an alternate agent in patients who are allergic to or cannot tolerate macrolides.
[6]TMP/SMZ is classified as an FDA Pregnancy Category C drug. It should not be given to pregnant women, nursing mothers, premature neonates, or infants <2 months of age.
[7]Treatment of pertussis is not an FDA approved use of azithromycin, but CDC has recommended it as first line treatment. Data on use of azithromycin in infants, 6months of age is limited, but CDC recommends it as preferred drug for pertussis in infants under 1 month of age. In infants 1-5 months, erythromycin and azithromycin were equally recommended.
[8]Whenever available the estolate preparation of erythromycin should be used.

Resistance to macrolides is rare. Penicillin-class drugs and first/second generation cephalosporins are not effective. Susceptibility testing is generally not done.

Case fatality:

In vaccinated populations, the fatality rate is very low (approximately 1% in infants younger than 2 months of age and less than 0.5% in infants 2 – 11 months of age). Fatalities typically are only seen in children under the age of 6 months. In unvaccinated populations, morbidity can be significant, but mortality is rare with appropriate medical care. However, because most of reported pertussis cases in infants are hospitalized, complication rates are likely to be representative of more severe illness.

Reservoir:

Humans are the only known hosts of *B. pertussis.*

Transmission:

Pertussis is transmitted via close contact with aerosolized droplets of respiratory secretions from infected persons. Transmission can also occur through contact with infected fomites. This disease is not thought to have airborne transmission. Pertussis is highly communicable, with secondary attack rates in susceptible household contacts as high as 90%. The majority of infectious patients are symptomatic; asymptomatic transmission is rare.

Incubation period:

The incubation period for pertussis is 7-10 days, with a range of 6 – 21 days.

Period of communicability:

Patients are most contagious during the catarrhal stage and the first two weeks after cough onset (approximately three weeks from the initial onset of symptoms). Patients are considered non-infectious following 5 days of antibiotic therapy.

Susceptibility:

Susceptibility is universal in unimmunized persons. Females have a higher incidence of disease and mortality. Pertussis immunity typically wanes 5-12 years after vaccination or natural infection.

Epidemiology:

Outbreaks of pertussis typically occur every 3-4 years. The highest annual incidence of pertussis occurs among unvaccinated children aged <5 years. Secondary attack rates are approximately 80% to 90% among susceptible household contacts.

Recently, both national and Utah trends demonstrate an increasing age in pertussis cases. It is unclear whether this is a real trend, or if it is due to increased recognition, diagnosis, and reporting of pertussis in adolescents and adults. In 2006, almost 78% of all reported pertussis cases occurred in persons 15 years of age and older. It is hypothesized that widespread use of pertussis vaccine in children may be responsible for the shift in

reported cases to adolescents/adults. In vaccinated populations, fewer mothers have acquired immunity through natural infection and may be less likely to provide passive immunity to an infant through transfer of maternal antibody. This leaves children under the age of one year as a highly at-risk population.

Currently, Utah has the highest rate of pertussis in the United States. 778 cases of pertussis were reported to the Utah Department of Health in 2006 for an annual incidence rate of 30.1 per 100,000 population. According to provisional data from the CDC, the annual incidence rate of pertussis in the United States for 2006 was 4.3 per 100,000 population.

✓PUBLIC HEALTH CONTROL MEASURES

Public health responsibility:

- Prevent illness in high-risk individuals through disease investigation, administration of vaccine, and antimicrobial prophylaxis.
- Promote vaccination to reduce disease burden in the community
- Provide education to the general public (regarding disease transmission) and to clinicians (regarding disease diagnosis, reporting, and prevention)
- Monitor disease trends

Prevention:

The primary method of pertussis prevention is through vaccination.

Chemoprophylaxis:

Prophylactic antibiotics may reduce secondary transmission in household and other settings. However, due to the lack of evidence supporting this conclusion, high number of pertussis cases occurring despite widespread antibiotic chemoprophylaxis, and the risk of antibiotic resistance developing due to overuse of antibiotics, UDOH recommends focusing efforts to provide chemoprophylaxis on high-risk contacts.
High-risk contacts include:

- Infants under the age of 1;
- Pregnant women;
- Contacts who work with high-risk individuals (e.g., daycare workers, healthcare workers with direct patient contact, etc.);
- Inadequately immunized schoolchildren under the age of 7; and
- Individuals, including parents and siblings, living in the same household with other high-risk contacts.

NOTE: Other contacts can be provided antibiotics at the discretion of the Local Health Authority.

Vaccine:

Diphtheria vaccine is complexed with acellular pertussis and tetanus toxoid, also known as DTaP. Immunization should be initiated in infancy. The first 3 doses are given at 4-8 week intervals beginning at 6-8 weeks of age; a fourth dose should be 6-12 months after

the third dose; and a fifth dose given at 4-6 years of age, but prior to school entry. This dose is not necessary if the fourth dose is given at 4 years or later.

Adults should receive vaccine specifically formulated with reduced concentration of diphtheria toxoid (Tdap). Active protection for adults should be maintained by administration of this vaccine every 10 years.

Isolation and quarantine requirements:

Isolation: Non-hospitalized patients with pertussis should remain out of school or childcare settings until they have received five days of appropriate antibiotic therapy, or, if not treated, until 21 days after the onset of symptoms. Voluntary isolation from work and other settings where close contact may transmit the disease is desirable. Such restriction of activity would be very difficult to legally enforce if involuntary.

Hospital: Hospitals should follow droplet precautions for five days of appropriate antibiotic therapy, or, if not treated, until 21 days after the onset of symptoms.

Quarantine: Susceptible contacts should remain out of school or childcare settings until 21 days after their last exposure or until the case and contacts have received 5 days of appropriate antibiotics.

R396-100-8. Exclusions of Students Who Are Under Exemption and Conditionally Enrolled Status.

(1) A local or state health department representative may exclude a student who has claimed an exemption or who is conditionally enrolled from school attendance if there is good cause to believe that the student has a vaccine preventable disease and:

(a) has been exposed to a vaccine-preventable disease; or

(b) will be exposed to a vaccine-preventable disease as a result of school attendance.

(2) An excluded student may not attend school until the local health officer is satisfied that a student is no longer at risk of contracting or transmitting a vaccine-preventable disease.

✓CASE INVESTIGATION

Reporting:

If pertussis is suspected, it should be reported to the local health department or the Utah Department of Health.

Case definition:

Pertussis *(Bordetella pertussis)* (Whooping Cough) (1997):

Clinical Case Definition

A cough illness lasting at least 2 weeks with one of the following:

- paroxysms of coughing,
- inspiratory "whoop," or
- post-tussive vomiting,

Without other apparent cause (as reported by a health professional).

Laboratory Criteria

- Isolation of *Bordetella pertussis* from clinical specimen, or
- Positive polymerase chain reaction (PCR) for *B. pertussis*

Case Classification

Probable: A case that meets the clinical case definition, is not laboratory confirmed, and is not epidemiologically linked to a laboratory-confirmed case.

Confirmed: A case that is culture positive and in which an acute cough illness of any duration is present; or a case that meets the clinical case definition and is confirmed by positive PCR; or a case that meets the clinical case definition and is epidemiologically linked directly to a case confirmed by either culture or PCR.

Comment

The clinical case definition above is appropriate for endemic or sporadic cases. In outbreak settings, a case may be defined as a cough illness lasting at least 2 weeks (as reported by a health professional). Because direct fluorescent antibody testing of nasopharyngeal secretions has been demonstrated in some studies to have low sensitivity and variable specificity (5, 6), such testing should not be relied on as a criterion for laboratory confirmation. Serologic testing for pertussis is available in some areas but is not standardized and, therefore, should not be relied on as a criterion for laboratory confirmation. Both probable and confirmed cases should be reported nationally.

Case investigation process:

Cases of pertussis should be managed as follows:

- Encourage appropriate laboratory testing.
- Ensure appropriate antibiotic treatment.
    - Generally recommended for those who are within three weeks of the onset of their illness.
    - Infants under the age of 1, pregnant women, and persons with ongoing, close contact with infants under the age of 1 or pregnant women (e.g., daycare workers, pediatricians) should be treated regardless of duration.
- Isolation should be imposed until 21 days after the onset of symptoms or 5 days after appropriate antibiotic therapy is begun.
- All case contacts should be identified and appropriately managed (explained in detail below).

Outbreaks:

Given the increasing numbers of pertussis cases that are reported, local health departments must use their judgement on determining when it is justified to declare an outbreak. However, formally an outbreak is defined as 2 or more cases within 42 days of each other. Declaration of an outbreak can be useful to elicit media coverage and support from physicians for improved interventions including case detection, reporting, and administration of prophylaxis and treatment. When an outbreak is declared, additional public health resources may need to be allocated to control the situation. Local health departments are urged to consult with the Utah Department of Health during outbreaks in order to develop situation-specific control measures and identify additional resources. Additional measures to limit transmission may be appropriate in outbreak settings. An epidemiologically linked case is one in which the patient has had contact with one or more persons who have or had the disease, and transmission of the agent by the usual modes of transmission is plausible. A case may be considered epidemiologically linked to a laboratory-confirmed case if at least one case in the chain of transmission is laboratory confirmed.

Identify case contacts:

Close contacts are defined as persons who share a confined space (<6 feet) for more than 1 hour with the patient during the infectious period (defined as a three week period, starting from the onset date identified above). Consider members of the following groups:

- Household and immediate family members (those who spend many hours together or sleep under the same roof);
- Those who have direct contact with respiratory secretions;
- Healthcare workers with extensive face-to-face contact with a patient who is coughing;
- Core groups of close friends, social contacts, boyfriends, girlfriends;
- Students sitting within 3 feet at school,
- Contacts at church activities and employment;
- Participants in extracurricular activities (such as fieldtrips); and
- Children attending after-school care or a playgroup.

Case contact management:

Asymptomatic Contacts

Chemoprophylaxis

Assure the following high risk contacts receive chemoprophylaxis:

- Infants under the age of 1;
- Pregnant women;
- Contacts who work with high-risk individuals (e.g., daycare workers, healthcare workers with direct patient contact, etc.);
- Inadequately immunized schoolchildren under the age of 7; and
- Individuals, including parents and siblings, living in the same household with other high-risk contacts.

Vaccination

For close contacts **<7 years of age** of pertussis cases:

- Assess immunization status;

- Recommend a fourth dose be given to all children who have received their third dose of DTaP 6 months or more before the exposure;
- Recommend a booster be given to all children who have received four doses of DTaP, unless the fourth dose was given in the past 3 years.
- *Note: asymptomatic contacts under the age of seven that have not received at least three doses of DTaP before the exposure shall be excluded from school/child care unless they elect to receive chemoprophylaxis.*

For close contacts **7-10 years of age** of pertussis cases:

- Currently, there is no vaccine licensed for use in children ages 7-10.
  For close contacts (10-18 years of age) of pertussis cases:
- Recommend vaccination with Tdap
- A 5-year interval between TD and Tdap is safe, but may cause a higher risk of local or systemic reactions; Tdap may be given after a shorter interval when the risk of transmission outweighs the risk of a reaction
- Adolescents with history of pertussis should still receive the vaccine
- *Note: There is only one vaccine approved for 10 year olds.*

For close contacts **>18 years of age** of pertussis cases:

- Advise people of the availability of a licensed vaccine for adults
- ACIP recommends adults receive a single dose of Tdap to replace a single dose of Td for booster immunization
- Tdap may be given at an interval shorter than 10 years since receipt of last tetanus-toxoid containing vaccine to protect against pertussis (interval as short as approximately 2 years)
- Adults who have or will have close contact with an infant <12 months of age should receive a single dose of Tdap
- Women who received the last tetanus-toxoid containing vaccine ≥10 years earlier should receive Td during pregnancy in preference to Tdap
- Women who received the last tetanus-toxoid containing vaccine <10 years earlier should receive Tdap in the post-partum period, according to the routine recommendations for vaccinating adult contacts of infants <12 months of age
- Pregnant women who have not received the primary 3-dose series for tetanus should begin the series during pregnancy

Symptomatic Contacts

- Recommend all symptomatic contacts obtain medical evaluation including confirmatory laboratory testing and antibiotic treatment if pertussis is identified.
- If symptomatic contacts refuse to obtain medical evaluation, consider providing antibiotic therapy.

✓REFERENCES

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